REMARKS

Prior to entry of the claim amendments presented above, claims 1-17 and 23-27 were pending in the application. Claims 1-17 and 23-27 were rejected. In the present amendment, claims 1, 24 and 25 have been amended and new claim 28 has been added. Accordingly, with entry of this amendment, claims 1-17 and 23-28 are now pending.

Claims Present for Examination

It appears that the Examiner has conducted examination on the basis of the claims as initially filed in the PCT Application, rather than the claims as amended during the International Phase. Applicants respectfully note that box 10 of the transmittal letter filed on entry into the U.S. National Phase was correctly marked. Accordingly, applicants respectfully request examination of the claims as amended during the International Phase. The claim amendment during the International Phase amended claim 1 to recite that the aryl group of R^1 is a substituted aryl group.

Specification

The specification has been amended to include the statement of priority. An abstract is attached hereto.

Claim Objections

Claims 11 and 17 are objected to because of formatting errors. Applicants traverse this objection. The alleged formatting error is nothing more than spacing caused by formatting claims with justified margins. The spacing is unavoidable when using justified margins with a list of long chemical names. Applicants submit that this spacing in no way could affect the reproducibility of these claims in electronic format and these claims fully comply with 37 CFR 1.52 and the MPEP. As the Examiner has not been able to cite how this formatting violates any rule, or why this formatting is unacceptable, applicants contend reformatting is not required. Reconsideration and withdrawal of this objection is respectfully requested.

Rejections Under 35 USC §112, Second Paragraph

Claims 3-11, 14-17 and 25 are rejected under 35 USC § 112, second paragraph, for being indefinite. The present claim amendments, as well as the amendment to claim 1 during the International Phase, render moot the rejections for lack of antecedent basis. For claim 25, applicants have amended this claim as suggested by the Examiner.

Rejections Under 35 USC §112, First Paragraph

Claim 24 is rejected for lack of enablement. Applicants deletion of the term "prophylaxis" renders this rejection moot.

Rejections Under 35 USC §102(b)

Claims 1, 2 and 23-27 are rejected under 35 USC § 102(a) as anticipated by GB 872447. Applicants respectfully traverse this rejection. As noted before, because of the amendment to claim 1 during the International Phase, this rejection is improper.

Rejections Under 35 USC §103(a)

Claims 1-17 and 24-27 are rejected under 35 USC § 103(a) as unpatentable over GB 872447 and EP0194112. Applicants respectfully traverse the rejection. During the International Examination applicants presented data showing the unexpected superiority of a substituted aryl group versus an unsubstituted aryl group. These data are reproduced below.

Applicants have unexpectedly found that compounds in which R^1 is a substituted aryl group exhibit an unexpected improvement in pharmacological activity *in vivo* in relation to compounds in which R^1 is an unsubstituted aryl group. In particular, improved pharmacological activity is demonstrated in the "Antagonism of 3-MPA-Induced Seizure" model in mice, which is described on pages 13-14 of the present specification.

In comparative experiments the results of which are described below, mice were administered vehicle or test compound (at a dose of 15 or 30mg/kg p.o.) 60 minutes before the administration of a bolus dose of 3-MPA, and the ED_{50} value (minimum effective dose) measured. The results of this test using the compound of Example 20 of the present specification and 1-carbamoyl-3-phenylazetidine (which is disclosed in GB-872447 in claim 11) are displayed in Table 1 below. The compound of Example 20 has R^1 = 4-

trifluoromethylphenyl and R^2 = H. 1-Carbamoyl-3-phenylazetidine is a compound wherein R^1 = phenyl and R^2 = H.

Table 1

Compound	Dose (mg/kg s.c.)	ED_{50} (Confidence limits)
Vehicle	-	18.5 (17.2-19.9)
Example 20	15	25.5 (22.8-27.4)*
Example 20	30	28.5 (26.4-30.6)*
1-carbamoyl-3-phenylazetidine	15	22.1 (19.0-25.6)
1-carbamoyl-3-phenylazetidine	30	22.9 (-)*

* = Significant Effect

The results clearly show that the minimum effective dose of Example 20 to block 3-MPA-induced seizures is less than or equal to 15 mg/kg, whereas the minimum effective dose for 1-carbamoyl-3-phenylazetidine is 30 mg/kg. Thus, the compound of Example 20 which contains a substituted aryl group is an unexpectedly more potent anti-convulsant agent than the prior art compound which contains an unsubstituted aryl group. It is submitted that this improvement could not have been predicted, whether in view of GB-872447 or a combination of GB-872447 and EP-0194112, and therefore the present invention is not obvious because of its unexpectedly superior properties that were not suggested by the prior art.

CONCLUSION

In view of the above remarks and amendments, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

If any additional extension(s) of time are required for the filing of this paper, applicants expressly petition for such extension(s) and authorize the Commissioner to charge any deficiency to Deposit Account 19-0741.

Respectfully submitted,

June 7, 2002
Date

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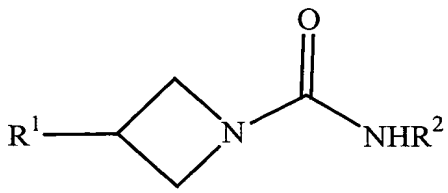
Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

ABSTRACT OF THE DISCLSOURE

1. (Amended Once) A compound of formula (1)



(1)

wherein

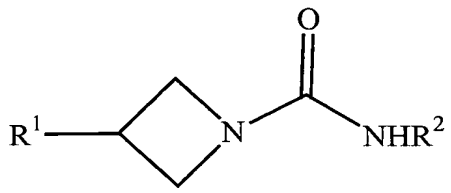
R^1 is substituted aryl; and

R^2 is hydrogen or alkyl wherein alkyl is defined as a branched or unbranced cyclic or acycli, saturated or unsaturated, substituted or unsubstituted hydrocarbyl radical;

and pharmaceutically acceptable addition compounds therefore.

Marked-Up Version of the Amended Claims

1. (Amended Once) A compound of formula (1)



(1)

wherein

R^1 is substituted aryl; and

R^2 is hydrogen or alkyl **wherein alkyl is defined as a branched or unbranched ,cyclic or acyclic, saturated or unsaturated, substituted or unsubstituted hydrocarbyl radical**; and pharmaceutically acceptable addition compounds therefore.

24. (Amended Twice) A method of treatment **[~~(including prophylaxis)~~]** of CNS disorders comprising administering to a patient in need of such treatment an effective dose of a compound according to claim 1.

25. (Amended Once) A method according to claim 24 wherein said method is for the treatment of anxiety, epilepsy, insomnia, **[~~including travel insomnia and insomnia associated with terminal illness,~~]** alcohol withdrawal syndrome, chronic and acute pain, neurodegenerative diseases, symptoms related to withdrawal from substance abuse or spasticity.